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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Jan 25  BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS  3  Jan 29  FSTA has been reloaded and moves to weekly updates
 NEWS  4  Feb 01  DKILIT now produced by FIZ Karlsruhe and has a new update
                  frequency
 NEWS  5  Feb 19  Access via Tymnet and SprintNet Eliminated Effective 3/31/02
 NEWS  6  Mar 08  Gene Names now available in BIOSIS
 NEWS  7  Mar 22  TOXLIT no longer available
 NEWS  8  Mar 22  TRCTHERMO no longer available
 NEWS  9  Mar 28  US Provisional Priorities searched with P in CA/CAplus
                  and USPATFULL
 NEWS 10  Mar 28  LIPINSKI/CALC added for property searching in REGISTRY
 NEWS 11  Apr 02  PAPERCHEM no longer available on STN.  Use PAPERCHEM2 instead.
 NEWS 12  Apr 08  "Ask CAS" for self-help around the clock
 NEWS 13  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS 14  Apr 09  ZDB will be removed from STN
 NEWS 15  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS 16  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS 17  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS 18  Apr 22  Federal Research in Progress (FEDRIP) now available
 NEWS 19  Jun 03  New e-mail delivery for search results now available
 NEWS 20  Jun 10  MEDLINE Reload
 NEWS 21  Jun 10  PCTFULL has been reloaded

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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FILE 'HOME' ENTERED AT 18:03:53 ON 24 JUN 2002

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FILE 'BIOSIS' ENTERED AT 18:04:22 ON 24 JUN 2002
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=> s dumoutier L?/au or louahed J?/au or Renauld J?/au
L1          431 DUMOUTIER L?/AU OR LOUAHED J?/AU OR RENAULD J?/AU

=> s l1 and stat?
L2           71 L1 AND STAT?

=> s l2 and TIF
L3           11 L2 AND TIF

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4            7 DUP REM L3 (4 DUPLICATES REMOVED)

=> dis l4 1-7 ibib abs

L4   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        2002:214923  CAPLUS
DOCUMENT NUMBER:         136:246402
TITLE:                   Isolated nucleic acid molecules which encode T cell
                         inducible factors (TIFs), the proteins
                         encoded, and uses thereof in prepn. of antibodies and
                         immunogens and in study of STAT activation
                         and interleukin-9 effects
```

INVENTOR(S): **Dumoutier, Laure**; Louhed, Jamila; **Renauld, Jean-Christophe**
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: U.S., 23 pp., Cont.-in-part of U.S. Ser. No. 178,973.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6359117	B1	20020319	US 1999-354243	19990716
US 6274710	B1	20010814	US 1998-178973	19981026
WO 2000024758	A1	20000504	WO 1999-US24424	19991018
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9965206	A1	20000515	AU 1999-65206	19991018
BR 9914777	A	20010703	BR 1999-14777	19991018
EP 1131333	A1	20010912	EP 1999-953231	19991018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6331613	B1	20011218	US 1999-419568	19991018
US 2001024652	A1	20010927	US 2000-751797	20001229

PRIORITY APPLN. INFO.: US 1998-178973 A2 19981026
US 1999-354243 A 19990716
US 1999-419568 A1 19991018
WO 1999-US24424 W 19991018

AB The invention involves isolation of nucleic acid mols., the expression of which is upregulated by interleukin-9. The amino acid sequences of the proteins which correspond to the nucleic acid mols. show some structural features of cytokines. The mols. are referred to as T cell inducible factors (**TIFs**). In addn. to the nucleic acid mols. and the proteins, various uses of the mols. are disclosed. One of the examples describes the use of the mols. in manuf. of antibodies which bind to the **TIF** protein. Such antibodies, monoclonal or polyclonal, constitute a further feature of the invention as do fragments of said antibodies, chimeric forms, humanized forms, and recombinant forms.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 7 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002183350 EMBASE
TITLE: Viral and cellular interleukin-10 (IL-10)-related cytokines: From structures to functions.
AUTHOR: **Dumoutier L.; Renauld J.-C.**
CORPORATE SOURCE: J.-C. Renauld, Ludwig Inst. for Cancer Research, UCL 74 59, Avenue Hippocrate, 74, B-1200 Brussels, Belgium. jean-christophe.renauld@bru.licr.org
SOURCE: European Cytokine Network, (2002) 13/1 (5-15).
Refs: 97
ISSN: 1148-5493 CODEN: ECYNEJ
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The anti-inflammatory and immunosuppressive activities of IL-10 have been extensively studied during the last 10 years. More recently a series of new cytokines, structurally related to IL-10, were described. This family includes mda-7, IL-19, IL-20, IL-**TIF**/IL-22, and AK155. Most of the biological functions of these cytokines remain to be unraveled but new data are coming out steadily. Although none of these "IL-10 homologs" mimics IL-10 activities, they are likely to be involved in inflammatory processes as well. mda-7, IL-19 and IL-20 form a subfamily within IL-10 homologs, based on conserved amino acid sequences, and on the use of shared receptor complexes. Functional studies have stressed the potential suppressing activity of mda-7 on tumor growth. As for IL-20, its overexpression in transgenic mice led to skin abnormalities, reminiscent of psoriatic lesions in humans. IL-**TIF**/IL-22 is a Th1 cytokine, and was shown to upregulate the acute phase reactant production by liver cells. Finally, for AK155, originally described as a gene induced upon T cell transformation by Herpes-virus saimiri, functional data are still lacking to determine its biological activities.

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:916420 CAPLUS
DOCUMENT NUMBER: 136:52731
TITLE: Isolated nucleic acid molecules which encode T cell inducible factors (**TIFs**), the proteins encoded, and uses thereof
INVENTOR(S): **Dumoutier, Laure**; Louhed, Jamila; **Renauld, Jean-Christophe**
PATENT ASSIGNEE(S): Ludwig Institue for Cancer Research, USA
SOURCE: U.S., 24 pp., Cont.-in-part of U.S. Ser. No. 354,243.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6331613	B1	20011218	US 1999-419568	19991018
US 6274710	B1	20010814	US 1998-178973	19981026
US 6359117	B1	20020319	US 1999-354243	19990716
US 2001024652	A1	20010927	US 2000-751797	20001229

PRIORITY APPLN. INFO.: US 1998-178973 A2 19981026
US 1999-354243 A2 19990716
US 1999-419568 A1 19991018

AB The invention involves isolation of nucleic acid mols., the expression of which are upregulated by interleukin-9. The amino acid sequences of the proteins which correspond to the nucleic acid mols. show some structural features of cytokines. In addn. to the nucleic acid mols. and the proteins, various uses of the mols. are disclosed. The mols. are referred to as T cell inducible factors.

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:291060 CAPLUS
DOCUMENT NUMBER: 132:333389
TITLE: Isolated nucleic acid molecules which encode T cell inducible factors (**TIFs**), the proteins encoded, and uses thereof
INVENTOR(S): **Dumoutier, Laure**; Louhed, Jamila; **Renauld, Jean-christophe**
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000024758	A1	20000504	WO 1999-US24424	19991018
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6274710	B1	20010814	US 1998-178973	19981026
US 6359117	B1	20020319	US 1999-354243	19990716
AU 9965206	A1	20000515	AU 1999-65206	19991018
BR 9914777	A	20010703	BR 1999-14777	19991018
EP 1131333	A1	20010912	EP 1999-953231	19991018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-178973 A 19981026
US 1999-354243 A 19990716
WO 1999-US24424 W 19991018

AB The invention involves isolation of nucleic acid mols. encoding **TIFs**, the expression of the **TIFs** which are upregulated by interleukin-9. The amino acid sequences of the **TIF** proteins which correspond to the nucleic acid mols. show some structural features of cytokines. In addn. to the nucleic acid mols. and the **TIF** proteins, use of the mols. for detg. effectiveness of interleukin 9, for stimulating **STAT** protein, for inhibiting activation of **STAT** protein are disclosed. Also provided are **TIF** inhibitor comprising antibodies and antisense mols. **TIF** mutein is useful for alleviating asthma or allergy.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2000:633242 CAPLUS
DOCUMENT NUMBER: 133:320857
TITLE: Human interleukin-10-related T cell-derived inducible factor: molecular cloning and functional characterization as an hepatocyte-stimulating factor
AUTHOR(S): **Dumoutier, Laure**; Van Roost, Emiel; Colau, Didier; **Renauld, Jean-Christophe**
CORPORATE SOURCE: Ludwig Institute for Cancer Research, Brussels Branch and the Experimental Medicine Unit, Christian de Duve Institute of Cellular Pathology, Universite Catholique de Louvain, Brussels, B1200, Belg.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(18), 10144-10149
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB IL-10-related T cell-derived inducible factor (IL-**TIF** or IL-21) is a new cytokine structurally related to IL-10 and originally identified in the mouse as a gene induced by IL-9 in T cells and mast cells. Here, the authors report the cloning of the human IL-**TIF** cDNA, which shares 79% amino acid identity with mouse IL-**TIF** and 25% identity with human IL-10. Recombinant human IL-**TIF** was found to activate signal transducer and activator of transcription factors-1 and -3 in several hepatoma cell lines. IL-**TIF** stimulation of HepG2 human hepatoma cells up-regulated the prodn. of acute phase reactants such as serum amyloid A, .alpha.1-antichymotrypsin, and haptoglobin. Although IL-10 and IL-**TIF** have distinct activities, antibodies directed against the .beta. chain of the IL-10 receptor blocked the induction of acute phase reactants by IL-**TIF**, indicating that this chain is a common component of the IL-10 and IL-**TIF** receptors. Similar acute phase reactant induction was obsd. in mouse liver upon IL-**TIF** injection, and IL-**TIF** expression was rapidly increased after lipopolysaccharide (LPS) injection, suggesting that this cytokine contributes to the inflammatory response in vivo.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 7 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000126044 MEDLINE
DOCUMENT NUMBER: 20126044 PubMed ID: 10657629
TITLE: Cloning and characterization of IL-10-related T cell-derived inducible factor (IL-**TIF**), a novel cytokine structurally related to IL-10 and inducible by IL-9.
AUTHOR: **Dumoutier L; Louahed J; Renauld J C**
CORPORATE SOURCE: Ludwig Institute for Cancer Research, Brussels, Belgium.
SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Feb 15) 164 (4) 1814-9.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
OTHER SOURCE: GENBANK-AJ249491; GENBANK-AJ249492
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000320
Last Updated on STN: 20000320
Entered Medline: 20000309

AB IL-9 is a Th2 cytokine active on various cell types such as T and B lymphocytes, mast cells, and eosinophils, and potentially involved in

allergy and asthma. To understand better the molecular mechanisms underlying the activity of this cytokine, we used a cDNA subtraction method to identify genes specifically induced by IL-9 in mouse T cells. One of the IL-9-regulated genes isolated by this approach turned out to encode a 180-amino acid long protein, including a potential signal peptide, and showing 22% amino acid identity with IL-10. This protein, designated IL-10-related T cell-derived inducible factor (IL-**TIF**), is induced by IL-9 in thymic lymphomas, T cells, and mast cells, and by lectins in freshly isolated splenocytes. Experiments concerning the mechanism regulating IL-**TIF** expression in T cells indicate that IL-9 induction is rapid (within 1 h), does not require protein synthesis, and depends on the activation of the Janus kinase (JAK)-**STAT** pathway. In vivo, constitutive expression of IL-**TIF** was detected by RT-PCR in thymus and brain, suggesting that the role of this new factor is not restricted to the immune system. Transfection of HEK293 cells with the IL-**TIF** cDNA resulted in the production of a glycosylated protein of about 25 kDa that was found to induce **STAT** activation in mesangial and neuronal cell lines. Further studies will have to address the possibility that some of the IL-9 activities may be mediated by IL-**TIF**.

L4 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:468282 BIOSIS
DOCUMENT NUMBER: PREV200000468282
TITLE: IL-**TIF** induces acute phase reactant production by hepatocytes through IL-10Rbeta.
AUTHOR(S): **Dumoutier, L. (1)**; Van Roost, E. (1); Colau, D. (1); **Renauld, J.-C. (1)**
CORPORATE SOURCE: (1) Brussels Branch, Ludwig Institute for Cancer Research, Brussels Belgium
SOURCE: Immunology Letters, (September, 2000) Vol. 73, No. 2-3, pp. 261. print.
Meeting Info.: 24th European Immunology Meeting of the European Federation of Immunological Societies (EFIS) Poznan, Poland September 23-26, 2000 European Federation of Immunological Societies
. ISSN: 0165-2478.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

=> dis his

(FILE 'HOME' ENTERED AT 18:03:53 ON 24 JUN 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 18:04:22 ON 24 JUN 2002
L1 431 S DUMOUTIER L?/AU OR LOUAHED J?/AU OR RENAULD J?/AU
L2 71 S L1 AND STAT?
L3 11 S L2 AND TIF
L4 7 DUP REM L3 (4 DUPLICATES REMOVED)

=> s (stat (1N) 3) (P) TIF?
L5 1 (STAT (1N) 3) (P) TIF?

=> s (stat (1N) 3) and TIF?
L6 2 (STAT (1N) 3) AND TIF?

=> dis l6 1-2 ibib abs

L6 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:264637 BIOSIS
DOCUMENT NUMBER: PREV200100264637
TITLE: Human IL-22 (IL-**TIF**) is a novel homolog of IL-10 that phosphorylates **STAT 3** in colon carcinoma cells expressing the IL-22R1 chain.
AUTHOR(S): Nagalakshmi, Marehalli L. (1); Parham, Christi (1); Rascle, Ann (1); Menon, Satish (1); Moore, Kevin (1); de Weal Malefyt, Rene (1)
CORPORATE SOURCE: (1) DNAX Research Institute, 901 California Ave, Palo Alto, CA, 94304 USA
SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1052. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB DNA database mining and bioinformatics have revealed the existence of several novel proteins that have 'IL-10 like' structural motifs. Human IL-22 is one such protein has been described as a hepatocyte stimulatory factor inducing the production of acute phase proteins from hepatocytes. IL-22 binds to its specific receptor comprising the IL-22 R1 and the IL-10R2 (CRF2-4) chains. This interaction leads to the activation of signal transducer and activator of transcription factors (STATs-1 and -3). Quantitative PCR analysis (TaqMan) showed that human IL-22 mRNA is expressed in activated T cell cDNA libraries. The IL-22R1 chain mRNA is highly upregulated in normal and diseased colon cell libraries. Expression of this receptor chain was at very low levels in resting and activated monocyte, T, B and dendritic cell cDNA libraries. The second receptor component, the IL-10R2 chain is known to be expressed ubiquitously. In addition, we have shown that human IL-22 obtained from transient transfections activates **STAT-3** in a colon carcinoma cell line, Colo205. Unstimulated cells expressed levels of IL-22R1 chain mRNA comparable to the human hepatoma cell line, HepG2. Levels of mRNA of the acute phase proteins - serum amyloid A, alpha - Antichymotrypsin and Haptoglobin were upregulated in IL-22 treated Colo205 cells. Future studies will be directed to identify the biological activities of this protein.

L6 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:440537 BIOSIS
DOCUMENT NUMBER: PREV200000440537
TITLE: Human interleukin-10-related T cell-derived inducible factor: Molecular cloning and functional characterization as an hepatocyte-stimulating factor.
AUTHOR(S): Dumoutier, Laure; Van Roost, Emiel; Colau, Didier; Renauld, Jean-Christophe (1)
CORPORATE SOURCE: (1) Brussels Branch and Experimental Medicine Unit, Ludwig Institute for Cancer Research, Christian de Duve Institute of Cellular Pathology, Universite Catholique de Louvain,

Avenue Hippocrate 74, B1200, Brussels Belgium
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (August 29, 2000) Vol. 97, No. 18, pp. 10144-10149. print.
ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB IL-10-related T cell-derived inducible factor (IL-**TIF** or IL-21) is a new cytokine structurally related to IL-10 and originally identified in the mouse as a gene induced by IL-9 in T cells and mast cells. Here, we report the cloning of the human IL-**TIF** cDNA, which shares 79% amino acid identity with mouse IL-**TIF** and 25% identity with human IL-10. Recombinant human IL-**TIF** was found to activate signal transducer and activator of transcription factors-1 and -3 in several hepatoma cell lines. IL-**TIF** stimulation of HepG2 human hepatoma cells up-regulated the production of acute phase reactants such as serum amyloid A, alphal-antichymotrypsin, and haptoglobin. Although IL-10 and IL-**TIF** have distinct activities, antibodies directed against the beta chain of the IL-10 receptor blocked the induction of acute phase reactants by IL-**TIF**, indicating that this chain is a common component of the IL-10 and IL-**TIF** receptors. Similar acute phase reactant induction was observed in mouse liver upon IL-**TIF** injection, and IL-**TIF** expression was found to be rapidly increased after lipopolysaccharide (LPS) injection, suggesting that this cytokine contributes to the inflammatory response in vivo.

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=> s (stat (1N) 3) (P) ((IL (1N) 21) or (IL (1N) 22))
L7 6 (STAT (1N) 3) (P) ((IL (1N) 21) OR (IL (1N) 22))

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8 3 DUP REM L7 (3 DUPLICATES REMOVED)

=> dis l8 1-3 ibib abs

L8 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:264637 BIOSIS
DOCUMENT NUMBER: PREV200100264637
TITLE: Human **IL-22** (IL-TIF) is a novel homolog of IL-10 that phosphorylates **STAT 3** in colon carcinoma cells expressing the IL-22R1 chain.
AUTHOR(S): Nagalakshmi, Marehalli L. (1); Parham, Christi (1); Rascle, Ann (1); Menon, Satish (1); Moore, Kevin (1); de Weal Malefyt, Rene (1)
CORPORATE SOURCE: (1) DNAX Research Institute, 901 California Ave, Palo Alto, CA, 94304 USA
SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1052. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB DNA database mining and bioinformatics have revealed the existence of several novel proteins that have 'IL-10 like' structural motifs. Human **IL-22** is one such protein has been described as a hepatocyte stimulatory factor inducing the production of acute phase proteins from hepatocytes. **IL-22** binds to its specific receptor comprising the **IL-22** R1 and the IL-10R2 (CRF2-4) chains. This interaction leads to the activation of signal transducer and activator of transcription factors (STATs-1 and -3). Quantitative PCR analysis (TaqMan) showed that human **IL-22** mRNA is expressed in activated T cell cDNA libraries. The IL-22R1 chain mRNA is highly upregulated in normal and diseased colon cell libraries. Expression of this receptor chain was at very low levels in resting and activated monocyte, T, B and dendritic cell cDNA libraries. The second receptor component, the IL-10R2 chain is known to be expressed ubiquitously. In addition, we have shown that human **IL-22** obtained from transient transfections activates **STAT-3** in a colon carcinoma cell line, Colo205. Unstimulated cells expressed levels of IL-22R1 chain mRNA comparable to the human hepatoma cell line, HepG2. Levels of mRNA of the acute phase proteins - serum amyloid A, alpha - Antichymotrypsin and Haptoglobin were upregulated in **IL-22** treated Colo205 cells. Future studies will be directed to identify the biological activities of this protein.

L8 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:261534 BIOSIS
DOCUMENT NUMBER: PREV200200261534
TITLE: The interleukin-2 (IL-2) receptor common gamma chain (gammac) is a required signaling component of the IL-21 receptor and supports IL-21-induced cell proliferation via JAK3.
AUTHOR(S): Habib, Tania J. (1); Weinberg, Kenneth I.; Kaushansky, Kenneth (1)
CORPORATE SOURCE: (1) University of Washington, Seattle, WA USA
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 818a. http://www.bloodjournal.org/. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The newly described lymphokines human and murine interleukin-**21** (IL-**21**) are 131 and 122 amino acid polypeptides produced by activated CD4+ lymphocytes. Structurally, **IL-21** is most closely related to IL-2 and IL-15, and although **IL-21** alone cannot support the proliferation of any subclass of lymphocytes, it profoundly affects the growth and activation state of B-, T and NK cells in concert with other lymphokines or stimuli. The biological effects of **IL-21** are mediated through a 538 amino acid class I member of the hematopoietic cytokine receptor superfamily (IL-21Ralpha). Although the complete IL-21R has not yet been defined, IL-21Ralpha is structurally similar to the beta subunit of the receptor for IL-2 and IL-15 (IL-2/15Rbeta) and thus, might utilize the

gammac chain for signaling. To test this hypothesis we used the gammac-deficient X-linked severe combined immunodeficiency B cell line JT, and JT cells reconstituted with gammac (JT-gammac). Moreover, we examined the functional requirement of both gammac and the gammac-associated Janus family tyrosine kinase 3 (JAK3) in IL-21-induced proliferation of pro-B-lymphoid cells engineered to express human IL-21Ralpha (BaF3/IL-21Ralpha). Using immunoprecipitation and Western blotting we found that IL-21 stimulated prominent tyrosine phosphorylation (Tyr-P) of JAK1 and JAK3 in BaF3/IL-21Ralpha, primary murine splenic B cells, and JT-gammac. In contrast, IL-21 failed to induce Tyr-P of JAK1 and JAK3 in JT cells. Moreover, STATs 1, 3 and 5 underwent Tyr-P in response to IL-21 in BaF3/IL-21Ralpha-, primary B- and JT-gammac cells but not in JT cells. To determine the functional role of gammac in IL-21 signaling, we conducted MTT proliferation assays with JT-gammac cells and found a specific proliferative response to IL-21; JT cells failed to respond to IL-21. Neutralizing monoclonal antibodies specific for the gammac chain effectively inhibited IL-21-induced growth of BaF3/IL-21Ralpha cells in an MTT assay, further supporting a functional role for this molecule in IL-21R signaling. Finally, the potent and specific JAK3 tyrosine kinase inhibitor WHI-P131 significantly reduced IL-21-induced proliferation of BaF3/IL-21Ralpha cells relative to the vehicle control. Taken together, these results definitively demonstrate that IL-21-mediated signaling requires the gammac chain of the IL-2 receptor, and indicate that JAK3 is an essential transducer of gammac-dependent survival and/or mitogenic signals induced by this cytokine.

L8 ANSWER 3 OF 3 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001023984 MEDLINE
DOCUMENT NUMBER: 20469498 PubMed ID: 10875937
TITLE: Interleukin (IL)-22, a novel human cytokine that signals through the interferon receptor-related proteins CRF2-4 and IL-22R.
AUTHOR: Xie M H; Aggarwal S; Ho W H; Foster J; Zhang Z; Stinson J; Wood W I; Goddard A D; Gurney A L
CORPORATE SOURCE: Department of Molecular Biology, Genentech, Inc., South San Francisco, California 94080, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Oct 6) 275 (40) 31335-9.
Journal code: 2985121R. ISSN: 0021-9258.
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LANGUAGE: English
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AB We report the identification of a novel human cytokine, distantly related to interleukin (IL)-10, which we term IL-22. IL-22 is produced by activated T cells. IL-22 is a ligand for CRF2-4, a member of the class II cytokine receptor family. No high affinity ligand has yet been reported for this receptor, although it has been reported to serve as a second component in IL-10 signaling. A new member of the interferon receptor family, which we term IL-22R, functions as a second component together with CRF2-4 to enable IL-22 signaling. IL-22 does not bind the IL-10R. Cell lines were identified that respond to IL-22 by activation of STATs 1, 3, and 5, but were unresponsive to IL-10. In contrast to IL-10, IL-22 does not inhibit the production of proinflammatory cytokines by monocytes in response to LPS nor does it impact IL-10 function on monocytes, but it has modest inhibitory effects on IL-4 production from Th2 T cells.

=> dis his

(FILE 'HOME' ENTERED AT 18:03:53 ON 24 JUN 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 18:04:22 ON 24 JUN 2002
L1 431 S DUMOUTIER L?/AU OR LOUAHED J?/AU OR RENAULD J?/AU
L2 71 S L1 AND STAT?
L3 11 S L2 AND TIF
L4 7 DUP REM L3 (4 DUPLICATES REMOVED)
L5 1 S (STAT (1N) 3) (P) TIF?
L6 2 S (STAT (1N) 3) AND TIF?
L7 6 S (STAT (1N) 3) (P) ((IL (1N) 21) OR (IL (1N) 22))
L8 3 DUP REM L7 (3 DUPLICATES REMOVED)

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	59.32	59.53
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WEST Search History

DATE: Monday, June 24, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR			
L15	(stat adj 3) and (IL adj 10)	3	L15
L14	(stat adj 3) and ((IL adj 21) or (IL adj 22))	2	L14
L13	(stat adj 3) same ((IL adj 21) or (IL adj 22))	0	L13
L12	(stat? or (IL adj 21) or (IL adj 22))	2108917	L12
L11	L10 and (stat? or (IL adj 21) or (IL adj 22))	7	L11
L10	(dumoutier)[IN] OR (louahed)[IN] or (renauld) [in]	154	L10
L9	(dumoutier)[IN] OR (louahed)[IN]	20	L9
L8	(ulex adj europaeus adj II) or UEAII	11	L8
L7	L6 and mbl	2	L7
L6	(stahl)[IN] OR (lekowski)[IN]	3181	L6
L5	(murine or mouse) same (inhibit$4) same (myoblast$4) same (different$4)	2	L5
L4	striamin	1	L4
L3	L2 and striamin	1	L3
L2	(wadhwa)[IN] OR (kaul)[IN] or (reddel)[in]	839	L2
L1	(wadhwa)[IN] OR (kaul)[IN]	816	L1

END OF SEARCH HISTORY

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 18:04:22 ON 24 JUN 2002

L1 431 S DUMOUTIER L?/AU OR LOUAHED J?/AU OR RENAULD J?/AU
L2 71 S L1 AND STAT?
L3 11 S L2 AND TIF
L4 7 DUP REM L3 (4 DUPLICATES REMOVED)
L5 1 S (STAT (1N) 3) (P) TIF?
L6 2 S (STAT (1N) 3) AND TIF?
L7 6 S (STAT (1N) 3) (P) ((IL (1N) 21) OR (IL (1N) 22))
L8 3 DUP REM L7 (3 DUPLICATES REMOVED)